## REMARKS

Amendments to the Claims

Claims 1, 3 , 7 and 8 have been amended to recite "a method of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints." Support for the amendment is found in the specification, for example, at page 57, lines 17-27. Further support is discussed below.

Claims 1 and 3 have been amended to recite "binds to human TNFα with an affinity of at least 1 x $10^8$ liter/mole measured as an association constant (Ka)." Support is found in the specification, for example, at page 60, line 25 to page 61, line 5 and Example X, particularly at page 80, line 24 to page 81, line 12.

No new matter has been added. Therefore, entry of the amendments into the application is respectfully requested.

Priority

The Examiner states that neither the priority applications nor the instant application provide a sufficient written description of a representative number of species to represent the entire genus of the pathology as currently claimed. The claims recite a pathology associated with increased TNFα concentrations relative to normal levels in the joints.

While Applicants disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to expedite prosecution, Applicants have amended Claims 1, 3, 7 and 8 to recite "a method of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints."

Support can be found in the specification, for example, at page 57, lines 17-27, which recites:

> The anti-TNF peptides, antibodies, fragments and/or derivatives of the present invention are useful for treating a subject having a pathology or condition associated with abnormal levels of a substance reactive with an anti-TNF antibody, in particular TNF, such as TNFα or TNFβ, in excess of levels present in a normal healthy subject, where such excess levels occur in a systemic, localized or particular tissue type or location in the body. Such tissue types can include, but are not limited to, blood, lymph, CNS,

> liver, kidney, spleen, heart muscle or blood vessels, brain or spinal cord white matter or grey matter, cartilage, ligaments, tendons, lung, pancreas, ovary, testes, prostate. Increased TNF concentrations relative to normal levels can also be localized to specific regions or cells in the body, such as joints, nerve blood vessel junctions, bones, specific tendons or ligaments, or sites of infection, such as bacterial or viral infections. (emphasis added)

Further support can be found in the specification at, for example, page 13, lines 1-8; page 13, line 26; page 58, line 1 to page 59, line 14; page 64, lines 3-26; page 100, line 25 to page 101, line 24; page 102, Table 5; page 104, Table 7 and Table 8; and page 105, line 8 to page 106, line 3. Further, Applicants' specification at page 64, lines 17-20 discloses that TNFα is involved in cartilage and bone destruction.

In addition, support is found in priority application 07/943,852, filed September 11, 1992, for example, at page 46, lines 21-29, which discloses that TNFα is involved in cartilage and bone destruction. Further support is found at page 13, lines 5-10; page 13, lines 24-29; page 40, line 25 through page 41, line 6; page 46, lines 6-17; page 47, lines 11-32; page 89, lines 12-27; page 90-91, Table 6 and Table 7; page 91, line 27 to page 92, line 1; and page 92, line 20 to page 93, line 2.

Thus, contrary to the Examiner's assertions, Applicants are not solely relying upon the disclosure of treating rheumatoid arthritis to support inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints.

The priority application 07/943,852 (filed September 11, 1992) provides sufficient written description for Applicants' claimed methods of treating patients with increased TNFα concentrations relative to normal levels in the joints, and Applicants are entitled to claim the benefit of it. This priority application has been properly referenced on page 1 of the specification in compliance with 35 U.S.C. § 120. Therefore, the priority of all pending claims is at least September 11, 1992.

Rejection of Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 under 35 U.S.C. § 112, first paragraph

The Examiner has rejected Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 under 35 U.S.C. § 112, first paragraph on the grounds that the specification as originally-filed does not contain a written description of "a pathology associated with increased TNFα concentrations relative to normal levels in the joints."

As indicated above, while Applicants disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to expedite prosecution, Applicants have amended Claims 1, 3, 7 and 8 to recite "a method of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints." As indicated above with regard to priority, support can be found in the specification, for example, at page 57, lines 16-27, and further support can be found in the specification at, for example, page 13, lines 1-8; page 13, line 26; page 58, line 1 to page 59, line 14; page 64, lines 3-26; page 100, line 25 to page 101, line 24; page 102, Table 5; page 104, Table 7 and Table 8; and page 105, line 8 to page 106, line 3. Further, Applicants' specification at page 64, lines 17-20 discloses that TNFα is involved in cartilage and bone destruction. Therefore, the application provides sufficient written description for Applicants' claimed methods.

Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 under 35 U.S.C. § 112, second paragraph

The Examiner has rejected Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 under 35 U.S.C. § 112, second paragraph as being indefinite in the recitation of "a pathology associated with increased TNFα concentrations relative to normal levels in the joints."

While Applicants disagree with the Examiner's position and reserve their rights to file continuing or divisional applications to pursue these claims, in order to expedite prosecution, Applicants have amended Claims 1, 3, 7 and 8 to recite "a method of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints." One of ordinary skill in the art would understand "inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints."

The claim terms are clearly defined. These claims, as amended, are definite because the terms of the claim are of general knowledge and a person of ordinary skill in the art would

understand the metes and bounds of inhibiting TNFα in a human with increased TNFα concentrations relative to normal levels in the joints. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 under 35 U.S.C. § 102(b)

The Examiner has rejected Claims 1, 3, 7-10, 14-16, 18-19 and 21-24 under 35 U.S.C § 102(b) as being anticipated by Le *et al.* (U.S. Patent No. 5,698,195).

Applicants respectfully disagree. The cited reference is Applicants' own priority patent. Le *et al.* (5,698,195) is not prior art under 35 U.S.C. § 102(b) because it was not published more than one year before Applicants' priority date. As indicated above, Applicants' amended claims are entitled to claim priority to U.S. Application Serial No. 07/943,852 (filed September 11, 1992). Le *et al.* (5,698,195) was filed over two years later, on October 18, 1994, and published on December 16, 1997.

Moreover, even if the claims were not entitled to the September 11, 1992 priority date, they would still be entitled to claim the benefit of the teachings of the cited reference, because it is Applicants' own priority patent. As disclosed on page 67, lines 2-19 of the priority application that granted as the Le *et al.* (5,698,195) Patent:

> The anti-TNF peptides, antibodies, fragments and/or derivatives of the present invention are useful for treating a subject having a pathology or condition associated with abnormal levels of a substance reactive with an anti-TNF antibody, in particular TNF, such as TNFα or TNFβ, in excess of, or less than, levels present in a normal healthy subject, where such excess or diminished levels occur in a systemic, localized or particular tissue type or location in the body. ... Increased or decreased TNF concentrations relative to normal levels can also be localized to specific regions or cells in the body, such as joints, nerve blood vessel junctions, bones, specific tendons or ligaments, or sites of infection, such as bacterial or viral infections. (emphasis added)

Therefore, this teaching also supports the claimed methods, particularly as amended. Therefore, the patent is not eligible as prior art under 35 U.S.C. § 102(b). Reconsideration and withdrawal of the rejection are respectfully requested.

Supplemental Information Disclosure Statement

A Supplemental Information Disclosure Statement (SIDS) is being filed concurrently herewith. Entry of the SIDS is respectfully requested.

## CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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